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Best evidence topic

Is laparoscopic ileocecal resection a safe option for Crohn's disease? Best evidence topic

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ABSTRACT

A best evidence topic was constructed according to a structured protocol. The question addressed was whether laparoscopic ileocecal resection for Crohn's disease is associated with higher morbidity rates in comparison to open surgery. From a total of 123 articles, 11 studies provided the best available evidence on this topic. Five observational studies, two randomized trials, three follow up studies and a meta-analysis were identified. The primary author, date and country of publication, study type, patient group characteristics, relevant outcome parameters and results of these papers were tabulated. Peri-operative morbidity was either similar between the laparoscopic and the open group, or favored the laparoscopic approach. Convalescence was consistently reported to be shorter in the laparoscopic treatment arm, at cost of longer duration of surgery. Limited evidence suggests lower incidence of small bowel obstruction and disease recurrence for laparoscopy, although follow up data are of poor quality. It may be concluded that laparoscopic ileocecal resection is a safe alternative approach to open surgery for uncomplicated Crohn's disease, provided laparoscopic expertise is available.

1. Introduction

A best evidence topic was constructed according to a structured protocol. This has been previously fully described.[1]

2. Clinical scenario

The case of a young male patient with uncomplicated Crohn's ileitis refractory to medical treatment is discussed in the weekly indication meeting of your department. Considering the available expertise in advanced laparoscopic surgery, you suggest offering a laparoscopic procedure to the patient. Colleagues from the gastroenterology department argue that the laparoscopic technique imposes risks to the safety of the anastomosis, because of the frail tissue and the long-term systemic therapy with steroids. You decide to search the literature yourself for the best available evidence on surgical approaches, and repeat the meeting before proceeding to surgery.

3. Three-part question

In [patients with Crohn's disease (CD)] is [laparoscopic surgery] associated with [higher surgical morbidity]?

4. Search strategy

Medline from inception up to July 2013: ([ileocolic resection] OR [ileocaecal resection] OR [caecectomy]) AND [laparoscopy]. Titles and abstracts were scrutinized; full texts of related articles were retrieved. Only studies written in the English language were considered.

5. Search outcome

One hundred and twenty three records were identified. Eleven articles were not in English, 61 were not relevant, 21 were case

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studies, 10 were review articles, 4 dealt with pediatric patient population, 3 did not report on postoperative complications, and 2 regarded robotic-assisted surgery. Eleven articles were considered to provide the best available evidence on this topic.

6. Results

The results of the 11 articles are summarized in the Table 1.

7. Discussion

Laparoscopic surgery offers a less invasive alternative to open ileocecal resection in patients with CD. The laparoscopic approach presumably reduces surgical stress and the possibility of anastomosis- and wound-related complications in immunosuppressed patients. Further, it may decrease the extent of adhesions, which is of specific importance in a patient population with high possibility of multiple operations for recurrent disease.[13] Nevertheless, although open surgery allows direct tissue manipulation and facile mechanical or hand-sewn anastomosis, laparoscopic ileocecal resection requires mobilization of the right colon and exteriorization of the terminal ileum and proximal ascending colon through a mini laparotomy. These manipulations may compromise the structural and functional integrity, and the blood supply of the bowel. Laparoscopy may further underestimate the extent of the disease, due to the loss of tactile feedback of the affected bowel.

Bemelman et al.[2] provided an early retrospective analysis of 78 patients with CD, subjected to laparoscopic or open surgery in the same time period, matched for demographic characteristics, but with different trends of administration of steroids (19 mg/day laparoscopic vs. 6 mg/day open; $p < 0.001$) and tube feeding (43% laparoscopy vs. 0% open; $p < 0.001$) in the perioperative period. Patient-oriented outcomes were similar for the open and the laparoscopic approach, although hospital stay favored laparoscopy. Their results may however be biased, due to this variation in perioperative care. Operating time favored the open approach, with a mean difference of 34 min ($p < 0.001$). Eshuis et al.[3] published an 8.5-year follow up report of this study, which demonstrated no difference in intestinal disease recurrence (23% laparoscopic vs. 22% open, p-value not significant). Mean follow up time was 8.3 years for the laparoscopic arm and 8.6 years for the open arm ($p = 0.38$).

Milsom et al. performed the first randomized trial on this subject.[4] This study had however multiple methodological shortcomings (no information on randomization method, not blinded, not reporting on dropouts, as-treated analysis) and fails to provide high quality evidence. Morbidity was 16% and 31% in the laparoscopic and the open treatment arms, respectively, a result which reached statistical significance ($p = 0.05$). The incidence of anastomotic leak was however similar (3% and 0%, respectively), as were the requirements of morphine analgesia. Duration of surgery favored the open approach (85 min vs. 140 min; $p < 0.00001$). The long-term follow up study by Stocchi et al.,[5] reporting on the outcome of 56 patients of the initial study population, demonstrated no difference in endoscopic recurrence and clinical recurrence requiring surgery.

In a high-quality, detailed retrospective report by Bergamaschi et al.,[6] 92 patients with CD were subjected to laparoscopic ($n = 39$) or open surgery ($n = 53$). Although the patient samples were treated in different time periods, they were matched for demographic, disease, and treatment characteristics. Thirty-day morbidity did not differ between the laparoscopic and the open group (10% vs. 9%, respectively). Two of 39 patients subjected to laparoscopic surgery required suture reinforcement of the anastomosis, due to air leak at control colonoscopy, which was only performed in the laparoscopic arm. Similar to previous reports, longer duration of surgery was registered for the laparoscopic approach (185 min vs. 105 min, $p < 0.001$). Duration of follow up of 84 patients was reported to be similar between the two groups at 5 years, with low possibility of dropout bias. Small bowel obstruction occurred in 11% of the laparoscopic group and in 35% of the open group ($p = 0.02$). Disease recurrence based on an objective disease activity index was registered in 28% and 29% of the laparoscopic and the open group, respectively ($p = 0.91$).

Lowney et al. reported on the perioperative and the 3-year outcome of 113 patients subjected to laparoscopic and conventional ileocecal resection.[7] Surgical morbidity was 19% and 34%, respectively; this difference however did not reach significance. Disease relapse requiring surgery occurred in 3% of the laparoscopic group and 13% of the open group. Strong evidence on more complex disease characteristics in the open treatment arm, with 11 cases of organ fistulization vs. one case in the laparoscopic group, must be taken into account.

In a more recent randomized trial of adequate quality,[8] Maartense et al. reported on 60 patients with CD. Longer duration of surgery was evident for the laparoscopic approach (115 vs. 90 min, $p = 0.003$). Thirty-day morbidity (10% vs. 33%, $p = 0.03$), return to normal diet (4 vs. 5 days, $p < 0.003$), and hospital stay (5 vs. 7 days, $p = 0.008$) favored laparoscopy. In the long-term follow up study by Eshuis et al.,[9] no difference in treatment outcomes was identified with regard to disease recurrence (39% vs. 45%, respectively), intestinal recurrence requiring surgery (7% vs. 12%, respectively) and reoperation for ileus (0% vs. 4% respectively) for the laparoscopic and the open approach.

The meta-analysis by Tilney et al., in 2006 provided pooled evidence of outcomes of low to high quality observational studies,[10] including the randomized trial by Milsom et al.[4] The analysis favored the open approach with regard to operative time (weighted mean difference 30 min, 95% confidence interval 11–48). Anastomotic leak and abscess formation was similar between groups. First bowel movement, return to normal diet and hospital stay favored the laparoscopic approach, heterogeneity being however evident in these outcome measures. The majority of studies were of poor quality, and sensitivity analysis of quality studies was undertaken, which validated the combined estimates of operating time, postoperative ileus and duration of hospital stay. Surgical morbidity was however not considered in this analysis.

A population-based analysis of the National Surgical Quality Program database by Lee et al. provided data on 644 laparoscopic and 1273 open ileocecal resections between 2005 and 2009.[11] Although both major (8% vs. 15%; $p < 0.0001$) and minor complications (9% vs. 13% open, $p < 0.0001$) presented with a lower incidence in the laparoscopic cohort, significant selection bias were inevitable and preclude generalization of results. This study provides however an estimate of operative morbidity in selected patients undergoing laparoscopic surgery for CD.

The most recent study by Makni et al.,[12] provides the outcome of 129 patients with similar demographic and disease characteristics between the laparoscopic and the open treatment arm. In accordance with previous reports, operating time for laparoscopic surgery was longer (158 min vs. 130 min, $p < 0.001$). Although overall morbidity was similar (8% laparoscopic vs. 11% open), there was a trend toward a higher incidence of anastomotic leak in the open group (0% vs. 8%, $p = 0.06$). The duration of postoperative ileus (2.9 vs. 3.4 days, $p = 0.02$) and hospitalization (7 vs. 9 days, $p = 0.001$) was shorter in the laparoscopic treatment group. Small bowel obstruction occurred in 5% and 9% of the laparoscopic and the open treatment arm, respectively (p not significant). Clinical recurrence required surgery in 19% of the open group and none in the laparoscopic group ($p = 0.001$). A longer follow up period for the open treatment arm should be considered (26 vs. 34 months).

Table 1
Best evidence papers.

Author, date and country, study type level of Evidence	Patient group	Outcomes	Key results	Comments
Bemelman WA[2] (2000) and Eshuis EJ[3] et al (2008) The Netherlands Retrospective cohort study (Level 3)	78 patients with CD • 30 lap (44 available to follow up) • 48 open (27 available to follow up) No difference in • Gender, age, BMI • Duration of disease • Prior surgery Mean steroid dosage higher and tube feeding more frequent in the laparoscopic group	• Morbidity • Operating time • Return to normal diet • First bowel movement • Hospital stay • Intestinal disease recurrence (8.5yrs follow up)	• 10% lap vs. 15% open (p ns) • 138min lap vs. 104 min open (p<0.001) • 5 days lap vs. 4 days open, (p ns) • 3 days lap vs. 4 days open (p ns) • 6 days lap vs. 10 days open (p=0.007) • 23% lap. vs. 22% open (p ns)	• Similar morbidity for the two approaches. • Similar long-term recurrence, similar follow up between study groups. • Moderate possibility of selection bias are introduced by significant differences in steroid usage and tube feeding between the study groups (suggest more intensive treatment in the laparoscopic arm).
Milsom JF[4] (2001) and Stocchi L[5] (2008) USA Randomized trial and follow up study (Levels 2 and 3)	60 patients with CD • 31 lap • 29 open No intention-to-treat analysis Long-term follow up (mean, 10.5 yrs) available for 56 patients (29 lap, 27 open)	• Operating time • Morbidity • Anastomotic leak • Use of morphine • Hospital stay • Colonoscopic, endoscopic recurrence, and recurrence requiring surgery • Requirement for multiple re-operations	• 140min lap vs. 85min open (p<0.00001) • 16% lap vs 31% open (p<0.05) • 3% lap vs. 0% open • 0.9mg/kg lap vs. 1.0mg/kg open (p ns) • 5 days lap vs. 6 days open (p ns) • No statistical difference between study groups • More frequent in the open group (p=0.006)	• Poor-quality randomized trial, but well-conducted follow up study. • Major complications similar, long-term outcome equivalent
Bergamaschi N[6] (2003) USA Retrospective cohort study (Level 3)	92 patients with CD • 39 lap • 53 open No difference in • Gender, age, BMI, ASA score • Duration of disease • Medical treatment • Prior surgery 84 patients (36 lap., 48 open) available at 5-year follow up	• 30-day morbidity • Operating time • Small bowel obstruction • Recurrence	• 10% lap vs. 9% open (p ns) • 185min vs. 105min (p<0.001) • 11% lap vs. 35% open (p=0.02) • 28% lap vs. 29% open (p ns)	• High quality retrospective study of prospectively maintained database with no evidence of selection bias. • 2 patients (5%) from the lap group required suture reinforcement of the anastomosis – air leak at control colonoscopy. • Control colonoscopy was only performed in the lap group. • 5-year outcome in favour of the lap approach in terms of obstructive ileus.
Lowney JK[7] (2005) USA Retrospective cohort study (Level 3)	113 patients with CD • 63 lap • 50 open Limited data on comparative patient demographics, evidence on more complex cases in the open arm	• Morbidity • Disease recurrence (3-year follow up)	• 19% lap vs. 34% open (p ns) • 3% lap. vs. 13% open	• Long-term follow up study suggesting a trend toward lower morbidity and recurrence rate for the laparoscopic arm, however with high possibility of selection bias.
Maartense S[8] (2006) and Eshuis EJ[9] (2010) The Netherlands Randomized trial and retrospective follow up study (Levels 2 and 3)	60 patients with CD • 30 lap • 30 open Long-term follow up (median, 6.7yrs) available for 55 patients (29 lap, 26 open)	• Operating time • 30-day morbidity • Return to normal diet • Hospital stay • Recurrence • Intestinal recurrence requiring surgery • Reoperation for small bowel obstruction	• 115min vs. 90min (p=0.003) • 10% lap vs. 33% open (p=0.03) • 4 days lap vs. 5 days open (p<0.003) • 5 days lap vs. 7 days open (p=0.008) • 39% lap vs. 45% open (p ns) • 7% lap vs. 12% open (p ns) • 0% lap vs. 4% open (p ns)	• High quality randomized trial (Jadad score 3) which favors the lap approach with regard to short-term patient-oriented outcomes at cost of longer operating time.
Tilney HS[10] (2006) United Kingdom Meta-analysis (Level 1)	783 patients with CD • 338 lap • 445 open included in 15 studies	• Operative time • Anastomotic leak • Intraabdominal abscess • First bowel movement • Return to normal diet • Hospital stay	• Favors open (WMD 30min, 95% CI 11-48) • Similar (OR 1.33, 95% CI 0.40-4.33) • Similar (OR 0.83, 95% CI 0.22-3.17) • Favors lap (WMD 0.58, 95% CI 0.03-1.12) • Favors lap (WMD 2.6 days, 95% CI 1.9-3.4) • Favors lap (WMD 3.0 days, 95% CI 2.0-3.9)	• Meta-analysis of observational and one randomized trial, providing evidence of poor to high-quality studies, with sensitivity analyses validating the results. • Heterogeneity was evident in duration of surgery, first bowel movement, return to normal diet and hospital stay.

Table 1 (*continued*)

Author, date and country, study type level of Evidence	Patient group	Outcomes	Key results	Comments
Lee Y[11] (2011) USA Retrospective database analysis (Level 4)	1917 patients with CD • 644 lap • 1273 open from the National Surgical Quality Insurance Program (NSQIP) database (2005-2009)	• Major complications • Minor complications	• 8% lap vs. 15% open (p<0.0001) • 9% lap vs. 13% open (p<0.0001)	• This cohort analysis demonstrates decreased incidence of minor and major complications in the lap arm; differences in demographic characteristics and co-morbidities introduce, however, significant selection bias.
Makni A[12] (2013) Tunisia Retrospective cohort study (Level 3)	129 patients with CD • 64 lap • 65 open Similar demographic and disease characteristics between study arms, follow up longer in the open group (26 vs. 34 months)	• Operating time • Morbidity • Anastomotic leak • First bowel movement • Hospital stay • Small bowel obstruction • Recurrence	• 158min lap vs. 130min open (p<0.001) • 8% lap vs. 11% open (p ns) • 0% lap vs. 8% open (p=0.06) • 2.9 days lap vs. 3.4 days open (p=0.02) • 7 days lap vs. 9 days open (p=0.001) • 5% lap vs.9% open (p ns) • 0% lap vs. 19% open (p=0.001)	• This retrospective analysis of a prospective database of patients with CD favors the laparoscopic approach in the vast majority of outcome parameters. • Evaluation of long-terms outcomes must take into account the difference in the duration of follow up of each study group

CD, Crohn's disease.
lap, laparoscopic.
ns, not significant.
OR, odds ratio.
WMD, weighted mean difference.
CI, confidence interval.

8. Clinical bottom line

Best available evidence suggests that laparoscopic ileocecal resection for CD provides at least similar perioperative outcomes as open surgery. Shorter convalescence is consistently reported, at the cost of longer operative time. Evidence is provided mainly by retrospective observational studies; a single randomized trial of adequate quality and a meta-analysis converge to these conclusions. Although reliable long-term data are largely lacking, studies with similar duration of follow up across treatment arms demonstrate similar or lower incidence of disease recurrence and less frequent events of small bowel obstruction for laparoscopic surgery. It may be concluded, that laparoscopic ileocecal resection is a safe alternative approach to open surgery for uncomplicated Crohn's disease, provided laparoscopic expertise is available.

Ethical approval

This is a review study; Ethical Approval was therefore not required.

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None.

Author contribution

Stavros A. Antoniou: Conception and design, data collection, data analysis and interpretation, drafting the article, final approval.

George A. Antoniou: Conception and design, data collection, data analysis and interpretation, revision for important intellectual content, final approval.

Oliver O. Koch: Conception and design, revision for important intellectual content, final approval.

Rudolph Pointner: Conception and design, revision for important intellectual content, final approval.

Frank A. Granderath: Conception and design, analysis and interpretation, revision for important intellectual content, final approval.

Conflict of interest

None.

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